## REMARKS

Applicants respectfully request reconsideration of the claims pending in this application. Claims 1, 2 7, 5, 6, and 9-11 are pending. Claims 3, 4, 8 and 12-14 are cancelled. Claims 1, 2 and 7 are allowable. This is an RCE application and the accompanying claims are identical to those presented in the papers faxed to the PTO December 17, 2004 – with the exception of claim 5(e) which is further amended.

The Examiner rejects claims 5, 6, 9 and 10 under 35 USC §112, first paragraph, because the Examiner believes the claimed polynucleotides, expression vectors, host cells and processes do not meet the written description requirements. In particular, the Examiner rejects claim 5(h), (now 5(e)), which recites an isolated nucleic acid that hybridizes to either strand of the polynucleotide that encodes amino acids 449-687 of SEQ ID NO:2 under conditions of moderate stringency. The recited conditions include 50% formamide and 6XSSC, at 42°C. with washing conditions of 60°C, 0.5XSSC, and 0.1% SDS. Further the isolated nucleic acid must encode a polypeptide that interacts with an IL-1R signal transduction factor. Independent claims 6, 9 and 10 recite expression vectors, hosts cells and processes that refer to the isolated polynucleotides of claim 5(e).

The Examiner is of the opinion that the claims encompass a genus of polynucleotides that may be structurally unrelated. In connection with this the Examiner contends that the claims do not require any particular conserved structure or other distinguishing feature. Further, the Examiner asserts that the specification fails to disclose the structural feature or correlate structure to function of the claimed genus of the nucleic acid, or a representative number of species of the claimed genus.

The Examiner distinguishes the present claims from the Example claims cited with approval in the PTO Written Description Guidelines because the Examiner points out that the example claim, Example 9, refers to an isolated nucleic acid that hybridizes under highly stringent conditions, not under conditions of moderate stringency. The Examiner's view is that an artisan would expect to yield structurally unrelated nucleic acid molecules and to produce substantial variations among species encompassed within the scope of the claims.

Applicants respectfully disagree and submit that the Examiner's rejection is improper. Of first note, the Examiner simply asserts that the claims encompass structurally unrelated polynucleotides and implies that no other limitations exist in the claims. The Examiner's conclusion appears to be based upon the Examiner's belief

that the recitation of moderate stringency removes all structural limitations from the claims at issue. The Examiner provides no sound scientific basis for this conclusion and this lack of factual basis results in an uninformed and improper rejection. There is no requirement in the law that the claims recite conserved structural features between the recited sequences and the sequences to which the recited sequence hybridizes. Furthermore, even if structurally unrelated nucleic acid molecules are produced, and as shown below this is very unlikely, the claims recite that the polynucleotides encode a polypeptide that interacts with an IL-1R signal transduction factor. This limitation narrows the scope of polynucleotides to those that are sufficiently structurally similar as to encode polypeptides having a specific activity.

In connection with claim 5(e), the Examiner's assertion that the specification does not disclose structural features of the claimed nucleic acid, the PTO has made it clear that the teaching required to support claims encompassing a number of molecules which are *further limited by reciting an operable activity*, (in this case, as amended such operable activity is the ability to interaction with an IL-1R signal transducing factor) is satisfied if the disclosure teaches how to make a candidate molecule and how to test the candidate molecule for the activity. *Ex parte Mark* 12 USPQ2d 1904 (Bd. Pat. App. & Int'f 1989). Applicants submit that the specification, in combination with the knowledge of those skilled in the art, teaches how to make the claimed variants and teaches how to test for the claimed interaction. Variants and fragments are discussed beginning on page 13 of the specification. In addition to the extensive teaching of mutagenesis techniques and polypeptide expression in the specification, those ordinarily skilled in the art are well aware of these techniques since they have been in common use for years and years, indeed decades. Suitable IL-1R transduction factors are described on page 11 and include MyD88, IRAK-1, IRAK-2, IRAK-M and TRAF6. Additionally, suitable binding assays are discussed beginning at page 31 and going forward. Any requirement that Applicants limit the claims to specifically recited polynucleotide sequences does not adequately protect Applicants in view of the scope of the invention and the disclosure. Thus, it is improper to demand that Applicants limit the claimed invention to specific structures when it is well within the knowledge of those skilled in the art to use routine experimental techniques to make and test for all of the claimed polynucleotides.

Finally, in the discussion below, Applicants use well-known hybridization modeling algorithms to demonstrate that the recited hybridization conditions, in fact, encompass polynucleotides with a sufficiently high identity to be comparable to a generic "high stringency" favored by the Examiner.

The algorithm is available from any molecular biology laboratory manual and is stated as follows:

Tm (melting temperature of a duplex) =79.8 C + 18.5 (log Na+) + .58 (% G+C) -.50 (% formamide)-L/780, where L is the nucleic acid length and G + C is the percent of G + C in the hybridizing nucleic acid.

Essentially this means that the temperature at which a nucleotide duplex comes apart is dependent upon ionic strength, the ratio of G+C in the nucleic acid, the length of the nucleic acid and the amount of formamide in the hybridization solution. Further, a 1% mismatch in DNAs lowers the Tm by 1.4 degrees C.

The conditions recited in the claims are as follows:

50% formamide and 6XSSC, at 42°C. with washing conditions of 60°C, 0.5XSSC, and 0.1% SDS

Hybridizing in 6XSSC and 50% formamide the Tm is:

Tm = 79.8 + 18.5 (log 0.99 ) + .58(49) – .5(50) –717/780 = 79.8 + 18.5(-.0044) + 28.4 - 25 – 0.92= 79.8-0.0814 +28.4 -25-0.92 = 82.2°C

However, there is a final wash step and this step determines the final degree of identity between the final captured nucleotides and the hybridizing nucleotide. After washing, the captured nucleotides the resulting identity between the captured nucleotide and the hybridizing nucleotide is higher and determines in the following manner.

The recited washing conditions are 60°C, 0.5XSSC and 0.1% SDS
Thus,
Tm = 79.8 + 18.5 (log 0.0032 + 0.082) + .58(49) – 0 –717/780 =
79.8 + 18.5(-1.07) + 28.4 – 0.92 = **87.5°**

Thus when 60°C is the washing temperature there is a mismatch of:

87.5°C - 60°C/1.4°C/% mismatch = **19.6 % mismatch**

The above demonstrates that given the recited conditions of hybridizing with the nucleotide that encodes amino acids 449-687 of SEQ ID NO:2, a total of 717 nucleic acids, at 42°C, 6XSCC and 50% formamide one can expect an identity difference of up to 28.4% or almost 73% of the nucleic acid used to perform the

hybridization. Following the wash step, the predicted overall lowest % identity between the captured nucleotide and the hybridizing nucleotide is greater than 80%. Applicants submit that a hybridization variant having 80% identity to the hybridizing polynucleotide and which has the functional capability of interacting with an IL-1R signal transduction factor fully meets the written description standard.

In the context of the present rejection, the Examiner strongly implies that should claim 5(c) recite "stringent" hybridization conditions, the claims would be allowable. Below Applicants apply stringent conditions described in the application to demonstrate that stringent conditions, are not sufficiently different in their final results to warrant the Examiner's rejection.

The relevant stringent conditions include a wash step of 0.2XSSC and 0.1% SDS at 68°C.

Thus,

$Tm = 79.8 + 18.5 (\log 0.033 + 0.0034) + .58(49) - 0 - 717/780 =$

$79.8 + 18.5(-1.17) + 28.4 - 0.92 = 85.7°$

Thus, with a 68°C wash:

85.7°C-68°C/1.4°/%mismatch = 12.62 % mismatch

and the lowest predicted identity between the captured nucleotides and the hybridizing nucleotide is about 87%. Thus, under the recited conditions the predicted identity between the captured and the hybridizing strands is about **80% while the predicted identity is less than 87% under stringent conditions.**

Without providing even the slightest analysis, and even without generally describing a rationale, the Examiner concludes that the relevant claims lack written description. Applicants contend that a proper rejection must be supported by a sound scientific basis and the present rejection lacks such a basis. Thus, the Examiner's rejection is improper and Applicants request that the Examiner find the relevant claims allowable.

Independent Claims 10 and 11 stand rejected under 35 USC §112, second paragraph, as being indefinite. In particular, the Examiner is of the opinion that claims 10 and 11 are unclear what protein is to be made by the process and the claims read on any proteins produced by the cell. Applicants traverse this rejection on the grounds that one skilled in the art understands the claim meaning. Claim 10 recites a process of preparing a polypeptide by culturing a host cell of claim 9 under conditions promoting expression of the polypeptide. The host cell of claim 9 comprises a vector

that includes a polynucleotide of claim 5. Similarly, claim 11 is a process for preparing a polypeptide by culturing a host cell transformed with a vector that contains a polynucleotide that encodes the polypeptide of SEQ ID NO:2.

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. . . . if the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, §112 demands no more. . . The degree of precision necessary for adequate claims is a function of the nature of the subject matter." (Miles Laboratories, Inc. v. Shandon Inc., 997 F.2d 870 (Fed. Cir. 1993). The current specification describes an IL-1R Accessory Protein, fragments and variants that maintain its activity, nucleotides that encode the IL-1R Accessory Protein and variant, processes for preparing the IL-1R Accessory Protein and variant and processing for using the proteins. Applicants submit that it is self evident as to what particular polypeptide is the subject of the process defined in Claims 10 and 11. The claim specifically describes the host cells, describes vectors and describes polynucleotides that encode the polypeptide of interest. One skilled in the art is sufficiently apprised of the polypeptide prepared by the claimed process by virtue of the specific vector and host cell utilized in the process and this is all that is required to meet the §112, second paragraph, requirement. In view of the above discussion, Applicants respectfully request that the Examiner find the claims allowable.

The Examiner rejects claim 5, part (e) (formerly (h)), 6, 9, and 10 under 35 USC §102(b), as being anticipated by Huang et al. (Proc. Natl. Acad. Scie. USA 94:12829-12832, 1997). Newly amended Claim 5(e) recites an isolated nucleic acid that hybridizes to either strand of a double-stranded DNA that encodes amino acids 449-687 of SEQ ID NO:2. In view of this amendment, Applicants believe that claim 5(e) is allowable and claims 6, 9, and 10, which refer to claim 5, are allowable. More particularly, isolated nucleic acids encompassed by claim 5(e) are restricted to those that hybridize to nucleic acids that encode amino acids 449-687 of SEQ ID NO:2 and which interact with an IL-1R signal transduction factor. In view of the above discussion relating to identity between the hybridizing DNA and the captured DNA, Applicants submit that the claimed nucleic acids do not include the nucleic acids described in the Huang et al. reference and Applicants request that this rejection be withdrawn.

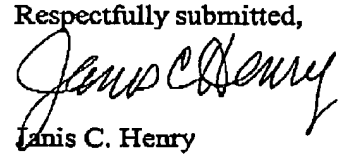
The Examiner further rejects claims 5, part (e) (formerly (h)), 6, 9, and 10 under 35 USC §102(e) as being anticipated by Cao et al. (US 6,280,955). The Cao et al. reference discloses the same IL-1R Accessory Protein variant described in the Huang et al. reference and the same arguments presented above with respect to the

Huang et al. reference are effective in overcoming this rejection. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Finally, the Examiner objects to claims 5, 6, 9 and 10 because unelected subject matter was present in claims 5. In view of the above amendment this objection is overcome.

Applicants submit that in view of the foregoing the claims in this application are in condition for allowance and a notice to the effect is respectfully requested.

Respectfully submitted,



Janis C. Henry
Attorney for Applicants
Reg. No. 34,347

Immunex Corporation
Law Department
1201 Amgen Court West
Seattle, WA 98119-3105
Telephone (206) 265-7000

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